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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/945,339	08/31/2001	Edmund K. Waller	05010.0087U1	1418

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NEEDLE & ROSENBERG, P.C.
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309-3915

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
10/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/945,339	WALLER ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *7-14 and 21-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. In view of the decision of BPAI on 09/13/07 to remand the application to the Examiner,

PROSECUTION IS HEREBY REOPENED.

2. Claims 1-58 are pending.

3. Claims 7-14 and 21-58 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. *Claims 1-6 and 15-20 are under consideration in the instant application.*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-6 and 15 –20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Waller (US Patent 5,800,539) in view of Sykes et al. (WO 99/25367) essentially for the same reasons set forth in the previous Office Action, mailed on 06/09/06.

Waller teaches a method of transplanting hematopoietic cells from a donor to genetically unrelated recipient that will inherently result in the enhancing immune reconstitution in the transplant recipient, comprising administering into the recipient in combination with the

hematopoietic cells an amount of mononuclear cells, which are treated so to reduce their ability to cause graft versus host disease (GvHD) effect, but which are retain their ability to facilitate engraftment of the hematopoietic cells in the recipient and administering to the recipient an effective amount of hematopoietic cells. (see entire document, Abstract and Claim 1 in particular). Waller also teaches that mononuclear cells are T cells, or natural killer (NK) cells, or mixture of T cells and NK cells (overlapping column 3-4 and claims 2-4 in particular). Waller also teaches that mononuclear cells are treated with chemotherapeutic drugs, including fludarabine (column 4, lines 66-67, column 5, lines 1-12 in particular). Waller teaches that said treatment sufficiently hinders the mononuclear cell proliferation such that they do not cause a lethal GvHD in the patient. It is noted that the main principle of operation of Waller is the ability of treated T cells to facilitate an engraftment of the hematopoietic cells in the recipient, while not inducing lethal GvHD (see column 4, lines 40-50 in particular). The crucial feature for operation of Waller is the viability of treated T cells. Waller explicitly stated that fludarabine treatment should sufficiently hinders the mononuclear cell proliferation but such that the mononuclear cells are effective in enhancing engraftment of the hematopoietic cells (see column 5, lines 25-35 in particular). It is thus the examiner position that a reasonable inference is that Waller's mononuclear cells retain a minimal ability to proliferate, but not enough to trigger a lethal GvHD effect.

Said feature, i.e. the ability of treated T cells to maintain minimal ability to proliferate in order to facilitate engraftment of the hematopoietic cells was known in the art at the time the invention was made. For example, Sykes et al., teach a method of a myeloreductive non-myeloablative treatment with fludarabine, the same type of treatment as claimed invention. Sykes et al., teach that for successful transplantation of hematopoietic cells from donor to recipient , it is essential that after treatment T cells are not completely depleted, thus so called graft-verses leukemia (GvL) effects of the non-depleted T cells help engraftment of donor hematopoietic cells (see page 10, lines 17-23, page 11, line 5-25 in particular). Sykes et al., specifically stressed that said treatment should not completely eliminated T cells (page 16, lines 2-11 in particular). In other words, Sykes et al., teach that said fludarabine-treated cells, should retain minimal ability to proliferate in a recipient in order to facilitate engraftment of hematopoietic cells.

It is noted that the instant Specification clearly disclosed that the crucial feature of the invention is that treatment with fludarabine should limit the ability of T cells to cause GvHD while retaining **their viability** (see page 5, line 6-15 and page 27, lines 14-25 in particular). The instant Specification also acknowledge that said treatment would sufficiently **hinders the mononuclear cell proliferation.** For example, on page 19, lines 15-20, it is explicitly stated that " The mononuclear cells are incubated with a sufficient concentration of the cytotoxic drug so as to substantially reduce their ability to cause GvHD. The sufficient concentration is that which **causes greater than 90 % inhibition of the proliferation of treated cells"** (emphasis added).

Thus, based on the teaching of the prior art , one skill in the art would understand that treatment with fludarabine while sufficiently hinders the mononuclear cell proliferation to prevent causing GvHD, still retain a minimal ability to proliferate. Thus, one skill in the art would understand that treated T cells should reduces their ability to cause GvHD while retaining their **viability** and their ability to facilitate engraftment of the hematopoietic cells.

Thus, all claimed elements were known in the prior art and one skill in the art could have combine the elements as claimed by known methods with no change in their respective function and the combination would have yield predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co v Teleflex Inc.*, 550U.S.-, 82 USPQ2d 1385, 2007).

Moreover, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Sykes et al., to those of Waller to obtain a claimed method of transplanting hematopoietic cells from donor to recipient, comprising administering into the recipient in combination with the hematopoietic cells an amount of mononuclear cells, which are treated so as to reduce their ability to cause graft versus host disease effect while retain their ability to proliferate in the recipient and facilitate engraftment of the hematopoietic cells in the recipient.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because one of ordinary skill in the art at the time the invention was made would deduce from the combined reference teaching that treatment of donor T cells in such a way as to retain not only their viability but also their ability to proliferate in the recipient, would be essential for successful engraftment of donor hematopoietic cells. Such treatment can be used in the method of transplantation hematopoietic cells taught by Walter.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

8. No claim is allowed

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

09/27/09